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Growth and Predictors of Growth Restraint in Moderately Preterm Children Aged 0 to 4 Years

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KEY WORDS
growth, moderately preterm-born children, growth restraint, growth prediction

ABBREVIATIONS
GA—gestational age
SGA—small for gestational age
HC—head circumference
Lollypop—Longitudinal Preterm Outcome Project
AGA—appropriate for gestational age

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WHAT'S KNOWN ON THIS SUBJECT: Early-preterm-born children often show growth restraint, and studies on small groups of moderately preterm-born children have found that they, too, are at risk. Both poor somatic growth and excessive weight gain can lead to long-term complications.

WHAT THIS STUDY ADDS: This study of 1123 children revealed that at age 4, growth regarding height and weight of moderately preterm-born children was restricted twice as often as that of term-born children. Being born small for gestational age and short mothers were identified as predictors of growth restraint.

abstract

OBJECTIVE: To describe growth in moderately preterm-born children, determine the prevalence of growth restraint at the age of 4, and identify predictors of growth restraint. We hypothesized that growth in moderately preterm-born children differs from growth in term-born children and that growth restraint is more prevalent in those born prematurely.

PATIENTS AND METHODS: This was a community-based cohort study of 1123 children born moderately prematurely (gestational age [GA]: 32–35⅙ weeks) between January 2002 and June 2003.

RESULTS: On average, we found that moderately preterm-born children were shorter and weighed less at each assessment during the first 4 years of life than their term-born counterparts. Thirty-two boys (5.6%) and 18 girls (3.8%) were growth-restricted in height, and 21 boys (3.4%) and 27 girls (5.8%) were growth-restricted in weight. Their growth in head circumference was normal compared with term-born children. In addition, growth restraint was associated with being small for GA at birth (odds ratio [OR] for height: 7.7 [95% confidence interval (CI): 2.9–20.4]; OR for weight: 9.5 [95% CI: 3.9–23.1]) and maternal height below −1 SD (OR for height: 4.9 [95% CI: 2.6–10.2]; OR for weight: 2.6 [95% CI: 1.3–5.2]). Poor head-circumference growth was associated with a low level of maternal education (OR: 5.3 [95% CI: 1.4–20.8]).

CONCLUSIONS: Growth in moderately preterm-born children significantly differs from that of term-born children. Predictors at birth are being small for GA, maternal height below −1 SD, and a low level of maternal education. The fact that growth in moderately preterm-born children may lag warrants close monitoring during routine practice. Additional research on prevention of growth restraint is needed. *Pediatrics* 2011;128:e1187–e1194

Worldwide, 5% to 13% of all children are born prematurely.[1–4] They form a relatively large group with serious medical, social, and economic implications for their parents, health care, and society.[1] A large majority of them (>85%) are moderately preterm-born children.[2,3]

Growth in early-preterm-born children (gestational age [GA] < 32 weeks) is studied widely. Findings consistently indicate that the prevalence of growth restraint in these preterm-born children is higher (10% to >20%) compared with that of children in the term-born population (2%).[5–7] Evidence also points to the persistence of intrauterine growth restraint in early-preterm-born children, as well as growth restraint starting after birth as a result of feeding problems, infections, and other neonatal complications. Poor growth in infancy puts the individual person at risk for growth restraint in adulthood and for metabolic complications.[5–13]

In contrast, despite the preponderance of moderately preterm-born children (GA of 32–35$^{6}/_{7}$ weeks), longitudinal information on their growth is scarce.[2,3] Moderately preterm-born children are born at the time when growth velocity is at its highest point ever. During these 4 weeks they gain much weight in the intrauterine environment.[7] Although evidence is lacking, it is likely that moderately preterm-born children miss this peak, which may subsequently lead to growth restraint, at least during the first years of life. The lack of information on growth also indicates that the impact of factors such as being small for GA (SGA) and maternal stature are not yet fully understood.

Our first aim was to provide a longitudinal description of growth in height, weight, and head circumference (HC) in moderately preterm-born children. Our second aim was to identify factors at birth that could serve as predictors of growth restraint at the age of 4 years. We hypothesized that the percentage of growth-restricted moderately preterm-born children would be greater compared with term-born children. Furthermore, we expected that the predictors of growth restraint identified at birth would add to the prediction of growth restraint at age 4.

METHODS

Study Design

Our study population was a subsample of the so-called Lollypop study. Lollypop (Longitudinal Preterm Outcome Project) is an extensive cohort study on growth, development, and general health of preterm infants (registered at www.controlled-trials.com [identifier ISRCTN80622320]). The design of the Lollypop study has been described in detail elsewhere.[14,15] In short, the Lollypop cohort consists of a large community-based sample of, in total, 1690 children born early and moderately prematurely before 36 weeks of gestation and 634 randomly selected term-born controls. The study combines retrospective data from medical records and parental questionnaires with measurements of height, weight, and HC of moderately preterm-born children.

Lollypop was approved by the local institutional review board, and written informed consent was obtained from all parents.

Sampling Procedure

Figure 1 provides an overview of the sampling procedure for moderately preterm-born children. The sample comprised almost all children born in

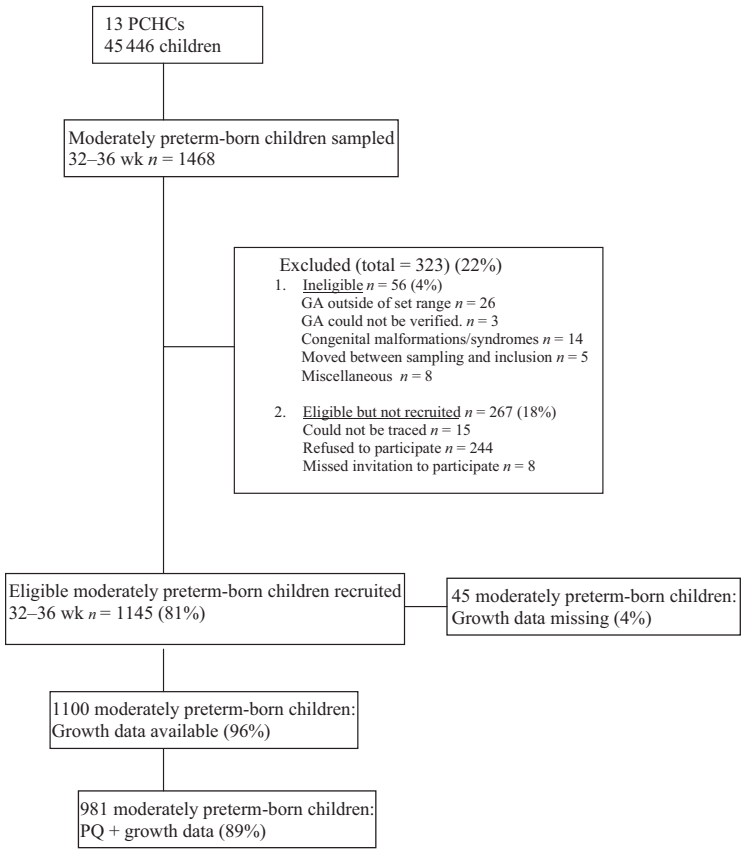

FIGURE 1
Sampling overview of the Lollypop. PCHC indicates preventive child health care services; MP, moderately preterm-born children; PQ, parental questionnaires; MR, medical records.

the northern, central, eastern, and southern regions of the country. Thirteen preventive child health care services in 2005 and 2006, covering ~25% of all children in the Netherlands, sampled all preterm children born between January 1, 2002, and May 31, 2003, at a GA of ≤36 weeks during a routine well-child visit at the age of 4 years. Attendance at this age was 97%.[16] Of 45 446 children, 1468 children were eligible on the basis of their GA. We excluded children with major congenital malformations and syndromes, but those with neurologic abnormalities were allowed (Fig 1). On the basis of national birth records, we concluded that this sample was fairly representative of the general population.

We recruited 1145 (response: 81%) moderately preterm-born children, and we collected growth data on 1123 of them (98%). When children were 4 years old, 981 (89%) parents completed the questionnaires. Mothers in the nonresponse group were more often of non-Dutch origin and had a slightly lower socioeconomic status on the basis of their level of education compared with responders. Apart from this, we found no significant differences according to response status.

Measures and Procedure

In >95% of the cases, GA was based on the date of last menstruation and confirmed by early ultrasound measurements. If not, estimates based on last menstrual date were checked with clinical estimates of gestation after birth. Children whose GA could not be defined beyond reasonable doubt were excluded.

Data on growth were obtained from records on routine assessments in both hospital and preventive child health care services settings from birth onward. During their first 4 years children routinely have ~15 well-child checkups during which height, weight, and HC (until the large fontanel is closed) are assessed. Height and weight were measured by using standardized measuring devices at every location. Up to the age of 15 months, the child was lying supine for the measurements; from 15 months onward, the child was standing. Weight was measured while the child was unclothed.

On average, for each preventive child health care services assessment growth values were missing for 20% of all children. Because of the larger number of assessments per child, we resolved this issue by estimating weight, height, and HC from the nearest measure available with the formula $(zx) = r(zy)$ (z score at age x = correlation times z score at age y, in which y represents the youngest age). In this way we reduced the number of missing values to 3.0%. Longitudinal graphs of each child were drawn on the basis of SD scores to correct registration errors.

Factors That Influence Growth

Data on predictors of growth were obtained from medical records and parental questionnaires. SGA was defined as a birth weight of less than −2 SDs according to the Kloosterman Dutch intrauterine growth curves.[17] Maternal height was requested in the parental questionnaire and measured while the mother was standing and wearing stockings. Paternal height was measured as well, but the majority of the fathers did not attend when we measured the child and mother. Therefore, we excluded paternal height from our analyses. In addition, the questionnaire provided data on ethnicity (based on the mother's country of birth), (the amount of) smoking during pregnancy, the mother's level of education, family income, duration of breastfeeding, multiple pregnancy, and conception by in vitro fertilization/intracytoplasmic sperm injection.

Statistical Analysis

To describe growth during the first 4 years of life, we assessed each child's height, weight, and HC at birth, on the day of the lowest postnatal weight during the first week of life, and at ages 1 month, 3 months (±1 week), 6 months (±2 weeks), 12 months (±2 weeks), 2 years (±1 month), 3 years (±1 month), and between 3½ and 4 years. HC was measured up to the age of 12 months, shortly before closure of the large fontanel, because the majority of HC growth occurs before the age of 1 year. Weight at birth was converted to SD scores according to the Dutch Kloosterman curve,[17] and height and HC were converted to SD scores according to the Usher and McLean curves.[18] Growth restraint after birth was defined as >2 SD scores below the median growth of the Dutch population, derived from the fourth Dutch nationwide growth survey.[19,20] We also collected (growth) data on a control group of term-born children. We compared this control group to the fourth Dutch growth survey and found the 2 groups to be comparable. Therefore, we decided to refer to this growth survey, which concerns a larger sample of term-born children.

Also, we assessed potential predictors for growth restraint (at the age of 4 years for height and weight and at the age of 1 year for HC) by using logistic regression. Factors that were univariately associated with growth restraint at $P < .20$, or factors that are, according to the literature, associated with growth restraint, were subsequently included in a multivariate (stepwise backward) logistic regression model. Factors in the latter category for the child were GA, SGA, gender, in vitro fertilization/intracytoplasmic sperm in-

jection, part of a multiple birth, and breastfeeding during the first 6 months of life, and factors for the mother were height, age, ethnicity, level of education, smoking during pregnancy, and family income.[10,21–24] Data from appropriate-for-GA (AGA) children were also analyzed separately to clarify any differences between AGA and SGA children. All analyses were performed with SPSS 16 for Windows (SPSS Inc, Chicago, IL).

RESULTS

Growth

For the 1123 moderately preterm-born children as a group, weight, height, and HC at birth were adequate. The occurrence of growth restraint in weight, height, or HC at birth (2.3% in a general population) was statistically comparable to that in the reference group of term-born children. Mean GA was 34⅞ weeks (SD: 1.0), and mean birth weight 2230 g (SD: 468). Our sample contained many multiples (29.6%), of whom 94.0% were twins. Of the singletons, 2.8% were SGA; of the multiples, 2.6% were SGA. Table 1 provides detailed information on maternal and child characteristics. Overall, <2.0% of the data were lacking (except for maternal height [7.0%]).

After birth, at a mean age of 5.3 days, moderately preterm-born children showed an average 8.0% maximum decrease in their birth weight, whereas during the first weeks of life, their height and HC did not change. After the initial decrease, weight increased within a narrow range up to the age of 6 months. From then on the range became wider and remained stable between the ages of 2 to 4 years. This pattern was similar for boys and girls, although girls' means were lower than the boys' means. Mean weights and heights at the ages of 1, 2, and 3 years are listed in Appendix 1. At the age of 4 years (mean: 3.9 years), moderately preterm-born boys weighed 16.9 ± 2.3 kg (mean ± SD), and moderately preterm-born girls weighed 16.0 ± 2.4 kg. Compared with term-born boys, who weighed 17.2 ± 2.1 kg, the preterm boys were 0.15 SD lighter ($P = .09$); compared with term-born girls, who weighed 16.7 ± 2.05 kg, the preterm girls were 0.25 SD ($P < .01$) lighter.

TABLE 1 Maternal and Child Characteristics

	Boys	Girls	Total
Total, *n* (%)	637 (57.0)	486 (43.0)	1123 (100.0)
Gestational age, *n* (%)			
32 wk	73 (11.5)	58 (11.9)	131 (11.7)
33 wk	131 (20.6)	98 (20.2)	229 (20.4)
34 wk	173 (27.2)	135 (27.8)	308 (27.4)
35 wk	260 (40.8)	195 (40.1)	455 (40.5)
Maternal height, *n* (%)			
Less than −2 SDs	38 (6.0)	35 (7.2)	73 (6.5)
−2 to −1 SDs	109 (17.1)	88 (18.1)	197 (17.5)
−1 to 1 SD	376 (59.0)	278 (57.2)	654 (58.2)
1 to 2 SDs	56 (8.8)	36 (7.4)	92 (8.2)
More than 2 SDs	11 (1.7)	5 (1.0)	16 (1.4)
Unknown	47 (7.4)	44 (9.1)	91 (8.1)
Smoking during pregnancy, *n* (%)			
No	483 (75.8)	378 (77.8)	861 (76.7)
1–5 cigarettes per d	64 (10.0)	38 (7.8)	102 (9.1)
6–10 cigarettes per d	44 (6.9)	29 (6.0)	73 (6.5)
>10 cigarettes per d	31 (4.9)	31 (6.4)	62 (5.5)
Ethnicity, *n* (%)			
Dutch	580 (91.1)	453 (92.2)	1033 (92)
Ex-colonial			
Dutch Antillean/Aruban	2 (0.3)	1 (0.2)	3 (0.3)
Suriname	5 (0.8)	5 (1.0)	10 (0.9)
Labor immigrant			
Turkish	4 (0.6)	1 (0.2)	5 (0.4)
Moroccan	9 (1.4)	3 (0.6)	12 (1.1)
Other non-Dutch			
Asian	8 (1.3)	6 (1.2)	14 (1.2)
African	6 (0.9)	4 (0.8)	10 (0.9)
Other	23 (3.6)	13 (2.7)	36 (3.2)
Maternal age, *n* (%)			
<20 y	10 (1.6)	5 (1.0)	15 (1.3)
20–35 y	565 (88.7)	428 (88.1)	993 (88.4)
>35 y	61 (9.6)	50 (10.3)	111 (9.9)
Family income, *n* (%)			
Low	51 (8.0)	28 (5.8)	79 (7.0)
Moderate/high	578 (90.7)	448 (92.2)	1026 (91.4)
Maternal level of education, *n* (%)			
Low	203 (31.9)	147 (30.2)	350 (31.2)
Moderate/high	425 (66.7)	329 (67.7)	754 (67.1)
In vitro fertilization/intracytoplasmic sperm injection, *n* (%)			
No	588 (92.3)	437 (89.9)	1025 (91.3)
Yes	42 (6.6)	44 (9.1)	86 (7.7)
Birth weight, median (SD), g	2291 (475)	2172 (448)	2240 (468)
SGA (<2nd percentile), *n* (%)			
No	614 (96.4)	479 (98.6)	1093 (97.3)
Yes	23 (3.6)	7 (1.4)	30 (2.7)
Multiple, *n* (%)[a]			
No	461 (72.4)	330 (67.9)	791 (70.4)
Yes	176 (27.7)	156 (32.1)	332 (29.6)
Breastfeeding (first 6 mo), *n* (%)			
No	545 (85.7)	426 (87.7)	971 (86.5)
Yes	85 (13.4	53 (10.9)	138 (12.3)

[a] The group of multiples consisted mainly of twins (94.0%), and the others were triplets and quadruplets (6.0%).

The increase in height showed a similar distribution for boys and girls, but the ranges remained stable over the entire period. Absolute height was again lower in girls. At 4 years, the mean height was 104 ± 4.3 cm for boys and 103 ± 4.1 cm for girls, which was 0.3 SD ($P < .01$) shorter compared with the term-born group from the national growth survey[19] (105.1 ± 4.0 cm) for boys and 0.2 SD ($P = .04$) shorter for girls (103.7 ± 4.1 cm).

HC growth was also similar for boys and girls. Again the girls' means were lower than the boys.' The ±2 SD scores varied little over time. At the age of 1 year, boys had a mean HC of 47.0 ± 1.3 cm and girls had a mean HC of 45.6 ± 1.3 cm, comparable to those in the reference group.

In short, the overall picture was a stable shift toward the lower side for weight and height attainment. HC growth was rapid after an initial period of growth failure, which resulted in comparable HC at 1 year of age.

Growth Restraint and Predictors

At the age of 4, in comparison with 2.3% of the term-born children from the national growth survey,[19] we found growth restraint in height in 50 children (4.6%; $P = .02$; SGA, $n = 8$; AGA, $n = 42$): 32 boys (5.6%; $P = .05$) and 18 girls (3.8%; $P = .35$).[25] We found an opposite gender distribution for weight in that 48 children (4.4%; $P = .04$; SGA, $n = 7$; AGA, $n = 41$) were underweight: 21 boys (3.4%; $P = .52$) and 27 girls (5.8%; $P = .02$). Growth restraint of HC was present in 10 children (1.2%; $P = .28$).

We found several factors at birth that predicted growth restraint (Table 2). In particular, SGA and maternal height below −1 SD were predictors of growth restraint in height and weight. Maternal age over 35 years also increased the child's risk of growth restraint. Of all the socioeconomic variables, we found that only a low level of maternal education was associated with poor HC growth. None of the other categories revealed significant associations, with the exception of ex-Dutch colonial ethnicity.

All significant factors in univariate analyses remained as independent predictors for growth restraint in the multivariate model (Table 3) except ethnicity and maternal age. SGA and short maternal height were most predictive for poor height and weight attainment in the long-term, whereas a low level of maternal education was the only predictive factor for HC growth. Analyses were repeated for AGA children only, but they did not yield any different results.

TABLE 2 Results of Univariate Logistic Regression Analyses for Low Height, Weight, and HC

	Height at 4 y Less Than −2 SDs, Crude OR (95% CI)	Weight at 4 y Less Than 2 SDs, Crude OR (95% CI)	HC at 1 y Less Than −2 SDs, Crude OR (95% CI)
GA			
35 wk (reference)	1.0	1.0	1.0
32 and 33 wk	1.1 (0.6–2.1)	1.2 (0.6–2.4)	1.0 (0.3–1.9)
34 wk	1.0 (0.5–2.0)	0.7 (0.3–1.5)	0.3 (0.04–2.7)
Gender, girls vs boys	1.4 (0.8–2.5)	0.6 (0.3–1.0)	3.0 (0.6–14.3)
Ethnicity			
Dutch (reference)	1.0	1.0	1.0
Ex-Dutch colonial	6.7 (1.7–25.3)[b]	7.3 (1.9–27.4)[b]	10.3 (1.2–9.1)[a]
Labor immigrant	1.6 (0.2–12.4)	1.7 (0.2–13.5)	9.3 (1.1–8.1)[a]
Other non-Dutch	1.3 (0.4–4.3)	1.9 (0.7–5.6)	
Maternal age			
20–35 y (reference)	1.0	1.0	1.0
<20 y	1.8 (0.2–14.0)	1.6 (0.2–12.6)	—
>35 y	2.2 (1.0–4.6)[a]	0.6 (0.2–2.0)	2.2 (0.5–10.4)
Maternal height			
−1 to 1 SD (reference)	1.0	1.0	1.0
Less than −2 SDs	8.5 (3.8–18.9)[b]	3.4 (1.5–4.1)[b]	—
−2 to less than −1 SD	5.1 (2.6–10.2)[b]	2.6 (1.3–5.2)[b]	12.3 (2.5–60.0)[a]
1 to 2 SDs	—	0.7 (0.2–3.0)	—
More than 2 SDs	—	—	—
Low maternal education level	1.6 (0.9–2.9)	1.0 (0.5–1.9)	5.3 (1.4–20.6)[a]
Low family income	1.5 (0.6–3.9)	0.9 (0.3–3.0)	—
Maternal smoking			
No (reference)	1.0	1.0	1.0
1–5 cigarettes per d	0.9 (0.3–2.7)	1.4 (0.5–3.6)	1.3 (0.2–10.4)
6–10 cigarettes per d	0.6 (0.2–2.7)	1.9 (0.7–5.1)	1.8 (0.2–14.6)
>10 cigarettes per d	1.5 (0.5–4.4)	1.8 (0.6–5.2)	2.1 (0.3–17.4)
IVF/ICSI, no vs yes	0.8 (0.2–2.6)	1.4 (0.6–3.7)	1.2 (0.2–9.9)
SGA, yes vs no	7.2 (2.9–17.7)[b]	9.3 (3.9–22.1)[b]	—
Multiple, no vs yes	1.2 (0.7–2.2)	1.9 (0.9–3.2)	2.6 (0.7–9.0)
Breastfeeding, yes vs no	0.5 (0.3–1.1)	0.7 (0.3–1.5)	1.2 (0.2–9.8)

OR indicates odds ratio; CI, confidence interval; IVF/ICSI, in vitro fertilization/intracytoplasmic sperm injection.
[a] $P < .05$.
[b] $P < .01$.

DISCUSSION

Our results indicate that moderately preterm birth was associated with poor longitudinal growth outcomes. At the age of 4 years, the risk for being underweight and/or comparatively short was substantially higher in moderately preterm-born children compared with term-born children. We also found several predictive factors as early as at birth that could be helpful in identifying moderately preterm-born children who are at risk of growth restraint.

Longitudinal height and weight attainment was inadequate in ~5% of all moderately preterm-born children. We found growth restraint 2.5 times more

TABLE 3 Factors Associated With Poor Growth at 4 Years (Height and Weight) and 1 Year (HC)

	Height at 4 y Less Than −2 SDs, OR (95% CI)	Weight at 4 y Less Than −2 SDs, OR (95% CI)	HC at 1 y Less Than −2 SDs, OR (95% CI)
SGA, unadjusted	7.2 (2.9–17.7)[a]	9.3 (3.9–22.1)[a]	—
SGA, adjusted	7.7 (2.9–20.4)[a]	9.5 (3.9–23.1)[a]	—
Maternal height, unadjusted			
−1 SD or higher	1.0	1.0	—
−2 or higher to less than −1 SD	5.1 (2.6–10.2)[a]	2.6 (1.3–5.2)[a]	—
Less than −2 SDs	8.5 (3.8–18.9)[a]	3.4 (1.5–4.1)[a]	—
Maternal height, adjusted			
−1 SD or higher	1.0	1.0	—
−2 or higher to less than −1 SD	4.9 (2.4–9.9)[a]	2.6 (1.3–5.3)[a]	—
Less than −2 SDs	7.0 (2.9–16.5)[a]	2.8 (1.1–7.4)[b]	—
Maternal educational level, unadjusted, low vs higher	—	—	5.3 (1.4–20.6)[a]
Maternal educational level, adjusted, low vs higher	—	—	5.3 (1.4–20.8)[a]

Shown are crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs). The ORs were adjusted for gestational age, ethnicity, maternal education level (low versus moderate/high), family income (low versus moderate/high), smoking during pregnancy (categorical), maternal age (categorical), in vitro fertilization/intracytoplasmic sperm injection (no versus yes), gender, being part of a multiple (singletons versus twins and versus triplets/quadruplets), and breastfeeding during the first 6 months of life (no versus yes).

[a] $P < .01$.

[b] $P < .05$.

often in moderately preterm-born children than in term-born children. The group of children who showed growth restraint consisted mainly of AGA children with poor longitudinal growth and some SGA children with lack of catch-up growth. Our findings are in line with those of Santos et al,[26] who found growth restraint in 4% to 9% late preterm-born children at the age of 2 years. Our data extend their findings to the age of 4 years, and our sample was considerably larger.

We found that the HC of moderately preterm-born children did not significantly differ from that of term-born children. At the end of the first year of life, only 1.2% of all moderately preterm-born children had a HC below −2 SDs. HC growth, however, did not occur during the first weeks. Evidence is lacking on whether this temporary delay in HC growth is associated with impaired neurodevelopmental outcome.[27,28] Further research is needed to elucidate this issue.

The predictors at birth that could help to identify children at highest risk for growth restraint (height and/or weight) were maternal height below −1 SD and SGA. Predictors for AGA children were comparable to those for the total group of moderately preterm-born children, which is highly relevant for clinical practice. Small maternal height is a well-known risk factor for poor height gain in a normal population.[21] This obviously also holds true for moderately preterm-born children. It was surprising that we found that in moderately preterm-born children short lengths of mothers were also associated with poor weight gain, albeit less strongly so than poor height attainment. To our knowledge, this has not been reported previously for prematurely born children. SGA had the strongest association with growth restraint, which reflects the lack of catch-up growth in this specific subgroup, as was also found among early-preterm-born children.[5,6]

Poor growth of HC during the first year was only associated with a low level of maternal education, as was described previously for term infants.[8,22] Low maternal education might be associated with a low maternal HC,[22] which suggests that the association we found has a genetic origin. We did not measure maternal HC, so this explanation needs additional study. We found no association between a low maternal education and poor height and weight gain. Similar findings were reported recently.[22]

We did not find other socioeconomic and demographic factors, including smoking during pregnancy, that influenced growth. Some of these factors, such as low family income, maternal age, and multiple birth, were associated with preterm birth,[3] but they apparently exerted no influence on long-term growth except through GA. With the social support system in the Netherlands, malnutrition associated with socioeconomic status is extremely rare. Smoking during pregnancy often precedes low birth weight,[29] but not in our sample, and it did not influence long-term growth.

Other factors that we expected to influence growth, such as a lower GA, breastfeeding during the first 6 months, gender, and in vitro fertilization/intracytoplasmic sperm injection, were not identified as predictors of growth restraint in our cohort. Breastfed children weighed less than formula-fed children at the age of 4, but the difference only reached significance at $P = .06$. A consistent finding in term-born populations is that breastfeeding prevents overweight in adulthood.[24,30] It is unknown whether long-term growth in moderately preterm-born children is affected by feeding practices. Finally, conception by artificial reproduction techniques did not result in poor growth, although others have reported that it is associated with lower birth weight.[23]

The major strengths of this study were our large sample of moderately preterm-born children, the community-based design, and the use

of multiple sources of information. We analyzed growth longitudinally, which is rarely done; most growth studies only use cross-sectional data. Finally, we had an inclusion rate of >80% and sufficient growth data on virtually all children.

Our study had some limitations. First, we found small differences in socioeconomic status between responders and nonresponders. Nevertheless, these differences were unlikely to have affected our findings, because socioeconomic status was not associated with long-term growth (weight and height). Second, we used the fourth Dutch nationwide growth survey as our reference.[19] It is based on children born shortly before 1997, whereas our cohort consisted of children born between 2002 and 2003. Height and HC have not increased since 1997, but weight has.[31] Thus, we could have underestimated growth restraint in the weight of moderately preterm-born children. Finally, retrospectively collected data on smoking during pregnancy may have been biased. However, Jaspers et al[32] revealed maternal recall of smoking during pregnancy to be good, even over 10-years of follow-up.

Our findings indicate that there is an urgent need to closely monitor growth in moderately preterm-born children, because they are at risk of growth restraint. In particular, this concerns those children whose mother is short, who were SGA, and whose mother had a low education level. Additional research is needed to prevent the short-term and long-term consequences of growth outside the normal range and its metabolic consequences, which may lead to optimization of feeding strategies for moderately preterm-born children and prevent both undernourishment in the neonatal period and overly rapid weight gain in the following months.

CONCLUSIONS

In this large, longitudinal study, growth of moderately preterm-born children significantly differed from the growth of term-born children; ~5% of the moderately preterm-born children were short and/or underweight at the age of 4 years. For the total group up to the age of 4, means for height and weight were below those of term-born children except at birth. HC growth was normal in the long-term. Maternal height of less than −1 SD and SGA were 2 factors present at birth that could be helpful in identifying the children at highest risk of growth restraint regarding height and/or weight. Only HC growth was influenced by a low level of maternal education. The development of descriptive, longitudinal growth charts for prematurely born children could be a useful tool for identifying growth outside the normal range and, thus, reduce subsequent complications of growth restraint.[8,33]

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APPENDIX 1 Median (Weight and Height) and Number of Children at −2 SDs at Ages 1, 2, and 3 Years

Age, y	Median Weight, kg (50th Percentile)	Median Height, cm (50th Percentile)	Weight at Less Than −2 SDs, *n* (%)	Height at Less Than −2 SDs, *n* (%)
Boys				
1	9.9	75.5	22 (3.5)	20 (3.1)
2	12.6	87.7	20 (3.1)	20 (3.1)
3	15.1	97.5	20 (3.1)	25 (3.9)
Girls				
1	9.0	73.4	29 (6.0)	20 (4.1)
2	11.8	86.2	25 (5.1)	18 (3.7)
3	14.3	96.4	23 (4.7)	13 (2.7)

Growth and Predictors of Growth Restraint in Moderately Preterm Children Aged 0 to 4 Years

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